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(54) Title: 2-PROPYLIDENE-19-NOR-VITAMIN D COMPOUNDS

(57) Abstract: 2-propylidene-19-nor-vitamin D compounds are disclosed as well as pharmaceutical uses for these compounds and methods of synthesizing these compounds. These compounds are characterized by high bone calcium mobilization activity and high intestinal calcium transport activity. This results in novel therapeutic agents for the treatment and prophylaxis of diseases where bone formation is desired, particularly osteoporosis, as well as autoimmune diseases such as multiple sclerosis, diabetes mellitus and lupus. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis. These compounds also increase both breaking strength and crushing strength of bones evidencing use in conjunction with bone replacement surgery such as hip and knee replacements.

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# INTERNATIONAL SEARCH REPORT

International Application No  
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## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07C401/00 C07F7/18 C07F9/53 A61K31/593 A61P19/08  
A61P17/06 A61P35/00 A61P35/02 A61P37/00 A61P1/00  
A61P29/00 A61P19/10

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07C C07F A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, BEILSTEIN Data, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>US 2002/087015 A1 (SICINSKI RAFAL R ET AL) 4 July 2002 (2002-07-04)</p> <p>Scheme 1 paragraphs '0012! - '0129! ----- -/--</p>	<p>1-11, 13-20, 22-46, 48-57, 59-67, 69-79, 81-92, 94-104, 106-109</p>

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

19 October 2004

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Int. Patent Application No.  
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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 392 071 B1 (SICINSKI RAFAL R ET AL) 21 May 2002 (2002-05-21)  column 2, line 34 - column 24, line 19	1-11, 13-20, 22-46, 48-57, 59-67, 69-79, 81-92, 94-104, 106-109
X	US 5 936 133 A (SICINSKI RAFAL R ET AL) 10 August 1999 (1999-08-10) cited in the application  column 2, line 25 - column 17, line 28	1-11, 13-20, 22-46, 48-57, 59-67, 69-79, 81-92, 94-104, 106-109
X	US 5 843 928 A (RAFAL SICINSKI R ET AL) 1 December 1998 (1998-12-01) cited in the application  column 2, line 24 - column 17, line 33	1-11, 13-20, 22-46, 48-57, 59-67, 69-79, 81-92, 94-104, 106-109

## INTERNATIONAL SEARCH REPORT

national application No.  
PCT/US2004/011059

### Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
**Although claims 36-109 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.**
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Int. Patent Application No.  
PCT/JP2004/011059

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2002087015 A1	04-07-2002	US 6392071 B1	21-05-2002
		US 5936133 A	10-08-1999
		US 5843928 A	01-12-1998
		US 2003181427 A1	25-09-2003
		US 2004167104 A1	26-08-2004
		AU 4790501 A	15-10-2001
		CA 2404548 A1	11-10-2001
		EP 1268416 A1	02-01-2003
		JP 2003529581 T	07-10-2003
		WO 0174766 A1	11-10-2001
		AT 223890 T	15-09-2002
		AU 714253 B2	23-12-1999
		AU 6280198 A	12-10-1998
		CA 2283829 A1	24-09-1998
		DE 69807852 D1	17-10-2002
		DK 970047 T3	11-11-2002
		EP 0970047 A1	12-01-2000
		ES 2179451 T3	16-01-2003
		JP 2001504135 T	27-03-2001
		NO 994398 A	10-09-1999
		NZ 337503 A	29-09-2000
		PT 970047 T	31-01-2003
		WO 9841501 A1	24-09-1998
US 6392071 B1	21-05-2002	US 5936133 A	10-08-1999
		US 5843928 A	01-12-1998
		AU 4790501 A	15-10-2001
		CA 2404548 A1	11-10-2001
		EP 1268416 A1	02-01-2003
		JP 2003529581 T	07-10-2003
		US 2002087015 A1	04-07-2002
		WO 0174766 A1	11-10-2001
		US 2003181427 A1	25-09-2003
		US 2004167104 A1	26-08-2004
		AT 223890 T	15-09-2002
		AU 714253 B2	23-12-1999
		AU 6280198 A	12-10-1998
		CA 2283829 A1	24-09-1998
		DE 69807852 D1	17-10-2002
		DK 970047 T3	11-11-2002
		EP 0970047 A1	12-01-2000
		ES 2179451 T3	16-01-2003
		JP 2001504135 T	27-03-2001
		NO 994398 A	10-09-1999
		NZ 337503 A	29-09-2000
		PT 970047 T	31-01-2003
		WO 9841501 A1	24-09-1998
US 5936133 A	10-08-1999	US 5843928 A	01-12-1998
		US 2002087015 A1	04-07-2002
		US 2003181427 A1	25-09-2003
		US 6392071 B1	21-05-2002
		US 2004167104 A1	26-08-2004
		AT 223890 T	15-09-2002
		AU 714253 B2	23-12-1999
		AU 6280198 A	12-10-1998
		CA 2283829 A1	24-09-1998
		DE 69807852 D1	17-10-2002

# INTERNATIONAL SEARCH REPORT

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PCT/US2004/011059

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5936133	A		DK 970047 T3 EP 0970047 A1 ES 2179451 T3 JP 2001504135 T NO 994398 A NZ 337503 A PT 970047 T WO 9841501 A1	11-11-2002 12-01-2000 16-01-2003 27-03-2001 10-09-1999 29-09-2000 31-01-2003 24-09-1998
US 5843928	A	01-12-1998	AT 223890 T AU 714253 B2 AU 6280198 A CA 2283829 A1 DE 69807852 D1 DK 970047 T3 EP 0970047 A1 ES 2179451 T3 JP 2001504135 T NO 994398 A NZ 337503 A PT 970047 T US 2002087015 A1 WO 9841501 A1 US 5936133 A US 2003181427 A1 US 6392071 B1 US 2004167104 A1	15-09-2002 23-12-1999 12-10-1998 24-09-1998 17-10-2002 11-11-2002 12-01-2000 16-01-2003 27-03-2001 10-09-1999 29-09-2000 31-01-2003 04-07-2002 24-09-1998 10-08-1999 25-09-2003 21-05-2002 26-08-2004